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10/519,950	12/29/2004	Alexis Collette	263996US2XPCT	7363
22850	7590	07/09/2008		
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER NEGIN, RUSSELL SCOTT	
			ART UNIT	PAPER NUMBER
			1631	
			NOTIFICATION DATE	DELIVERY MODE
			07/09/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/519,950	<b>Applicant(s)</b> COLLETTE ET AL.	
	<b>Examiner</b> RUSSELL S. NEGIN	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 April 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 91-111 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 91-111 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 April 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Comments***

Applicants' amendments and request for reconsideration in the communication filed on 1 April 2008 are acknowledged and the amendments are entered.

### ***Withdrawn Rejections***

All rejections previously set forth are hereby withdrawn in view of the cancellation of all previously pending claims. All rejections set forth below are necessitated by the amendment citing all new claims.

### ***Claim Rejections - 35 USC § 101***

The following rejection is necessitated by applicant's amendment:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 91-105 and 110-111 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The following analysis of facts of this particular patent application follows the analysis suggested in the "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility". Note that the text of the Guidelines is italicized.

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):

- The claimed invention “transforms” an article or physical object to a different state or thing.
- The claimed invention otherwise produces a useful, concrete and tangible result.

In the instant case, the claimed invention does not “transform” an article or physical object to a different state or thing because it is a method for high throughput analysis of data sets. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

*physical transformation “is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application.” AT&T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a “practical application,” the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is “useful, tangible and concrete.” The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)*

The question is thus whether the final result achieved by the claimed invention satisfies all three criteria of being useful, and concrete, and tangible.

Furthermore, the useful, tangible, and concrete result must be recited in the claim itself, rather than addressed in specification.

The instant claims are drawn to a method for analysis of data sets. However, as claimed, the method does not produce a tangible result. For example, the method as claimed may take place entirely within the confines of a computer or a human mind without any communication to the outside world and without using or making available for use, the results of the computation. Thus, the instant methods of the claims do not produce any tangible result. While the instantly rejected claim recite storing each smoothed set in a data file, it is possible that such data may only be accessible by other computer systems and not actual users. In this instance, the data files may be accessible to the computer program (which is not a user) DataExtractor (see page 72; lines 6-10).

Response to Arguments:

Applicant argues that the amendments and cancellation of the rejected claims overcomes the rejection of record. This is found to be persuasive; a new ground(s) of rejection necessitated by applicant's amendments is applied to the new set of claims.

***Claim Rejections - 35 USC § 112***

The following rejection is necessitated by applicant's amendments:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 91-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 91-111 contain the trademark/trade name ISEAPEAKS. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a source of an algorithm (software), but does not recite the algorithm itself. It is unclear what specific limitations/computations/steps are intended to be encompassed by the software, therefore the claims are indefinite. For purposes of further examination, the term ISEAPEAKS will be interpreted as a peak smoothing (software) algorithm.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following rejection is necessitated by applicant's amendments:

35 U.S.C. 102(b) Rejection #1:

Claims 91, 92, 96, 98-100 are rejected under 35 U.S.C. 102(b) as being anticipated by Sotak et al. [Analytical Chemistry, 1983, volume 55, pages 782-787].

Claim 91 is drawn to a method for analyzing data, comprising:

--obtaining multiple sets of raw data from a primary source, wherein each data set has peaks having a defined position and area;

--smoothing the peaks in each data set based on one or more user defined parameters using the ISEApeaks® software; and

--storing each smoothed data set in a data file.

Claim 92 is further limiting comprising assimilating the smoothed data from each data set into a peak database using ISEApeaks® software (i.e. a peak smoothing algorithm).

Claim 96 is further limiting wherein the multiple set of raw data are obtained from a high throughput analysis of data sets generally described by sets of peaks characterized by a position and an area.

Claim 98 is further limiting wherein particular profiles representing peaks are created in a form suitable for analysis.

Claim 99 is further limiting wherein the peak database is built.

Claim 100 is further limiting wherein the peak database is analyzed by at last one statistical tool.

The study of Sotak et al. describes software for quantitative analysis by carbon-13 Fourier Transform Nuclear Magnetic Resonance Spectrometry. Tables II through IV on page 784 of Sotak et al. describe high throughput analysis of peak position and area for a mixture of chemicals.

Tables II through IV of Sotak et al. show the use of bioinformatics tools to extract peak data sets and store them as profiles in data files. The tables act as databases on page 784 of Sotak et al.

The statistical tools used to analyze the peaks of Sotak et al. in Tables II through IV are the expected integral, the mean integral and the relative error.

One statistical tool that is used is approximating area under each peak using the techniques described on page 786 of Sotak et al. Such techniques serve to simplify or "smooth" the profile of each peak such that a relative area can be calculated under the peak. Consequently, the algorithms of Sotak et al. (page 786) serve the same function as smoothing the area under each peak. It should be noted that while the specific trademark ISEApeaks® is not taught in the instant prior art, the prior art performs the identical function of smoothing peaks as the ISEApeaks software.

Response to Arguments:



Applicant argues that the amendments and cancellation of the rejected claims overcomes the rejection of record. It is noted that the previous rejections have been withdrawn in view of cancellation of previously pending claims. In order to facilitate prosecution, however, arguments regarding Sotak et al. are addressed as follows. In response to the argument that Sotak et al. teaches only Fourier Transform and does not teach the instantly recited method, it is noted that Sotak et al. does teach all of the claimed limitations, including a peak smoothing algorithm, as set forth above.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is newly applied and necessitated by applicant's amendments:

35 U.S.C. 103 Rejection #1:

Claims 91-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Faure et al. [The Journal of Immunology, 1999, volume 163, pages 6511-6519] in view of Sotak et al. [Analytical Chemistry, 1983, volume 55, pages 782-787].

Claims 91, 92, 96, 98-100 are discussed above.

Claim 110 is drawn to the same method steps of claim 91 with the additional limitation of the preamble reciting that the purpose of the method is for analyzing data describing a T or B cell immune repertoire. Claim 111 is further limiting wherein the raw data describes CDR3 spectratypes.

The study of Faure et al. describes the tolerance of T cells through various different mechanisms. Figure 3 of Faure et al. on page 6514 shows various peak positions and areas obtained through high throughput analysis as a function various CDR3 sizes.

Figure 3 of Faure et al. illustrates a peak database.

The arrows in Figure 3 of Faure et al. illustrate the analysis of the peak database by statistical tools.

However, Faure et al. does not show actual smoothing of the peaks.

The study of Sotak et al. describes software for quantitative analysis by carbon-13 Fourier Transform Nuclear Magnetic Resonance Spectrometry.

One statistical tool that is used is approximating area under each peak using the techniques described on page 786 of Sotak et al. Such techniques serve to simplify or

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"smooth" the profile of each peak such that a relative area can be calculated under the peak. Consequently, the algorithms of Sotak et al. (page 786) serve the same function as smoothing the area under each peak.

It should be noted that while the specific trademark ISEApeaks® is not taught in the instant prior art, the prior art performs the identical function of smoothing peaks as the ISEApeaks software.

Claim 93 is further limiting wherein the raw data is obtained from a primary source comprising an electrophoretic sample. Figure 3 on page 6514 of Faure et al. illustrates data from an electrophoretic sample.

Claim 94 is further limiting wherein the multiple sets of raw data are obtained from an automated sequencer. The paragraph bridging pages 6512-6513 describes such an automated sequencing process.

Claim 95 is further limiting wherein the multiple sets of raw data are obtained from a sequencer and contain peaks that correspond to a CDR3 hypervariable region from the beta chain of a T cell receptor.

Figure 3 on page 6514 of Faure et al. and its caption illustrate a hypervariable region that correspond to a CDR3 hypervariable region of a T cell receptor.

Claim 97 is further limiting wherein at least one bioinformatic tool which is a raw data extraction program or a DNA automatic sequencer is used to extract and smooth peak data sets according to parameter filed and store them in data files.

The arrows in Figure 3 of Faure et al. illustrate the analysis of the peak database by statistical, bioinformatic tools.

Claim 101 is further limiting with the additional limitation that analysis of the peak database is used to determine prognostic or diagnostic criteria.

Figures 1 and 2 of Faure et al. illustrate the effect of age on proliferation of cells in various organs of the test mice.

Claim 102 is further limiting with the additional limitation that the prognostic and diagnostic criteria are used in the field of physiopathology.

Claim 103 is further limiting with the additional limitation that the criterion is useful in the field of immunotherapy.

Figures 1-3 of Faure et al. illustrate the physiopathology of T cell proliferation in mice.

Claim 104 is further limiting with the additional limitation that the method is a high throughput method for analysis of immune repertoires.

Figure 3 of Faure et al. illustrate an immune repertoire analysis (i.e. V $\beta$ 2, V $\beta$ 6, and V $\beta$ 13).

Claim 105 is further limiting with the additional limitation of starting with biological samples, which contain DNA or RNA fragments, purifying the DNA or RNA fragments.

Claim 106 is dependent from claim 105 with the additional limitations:

- synthesizing cDNA from purified RNA defining an immune repertoire;
- amplifying the cDNA by PCR or SDA methods by using oligonucleotides specific for antigen specific receptor genes ;
- labeling the amplified DNA for detection by performing a runoff extension step with J or C specific oligonucleotide labeled with a fluorescent drug;
- separating by electrophoresis each labeled amplified DNA on an automatic sequencer thus obtaining a set of electropherograms;
- identifying peaks in said set of electropherograms by determining their position and area that correspond to labeled amplified DNA.

Claims 107 and 108 are further limiting wherein the oligonucleotides specific for an antigen specific receptor gene are from the variable (V), junctional (J) and/or constant (C) regions of an immunoglobulin receptor gene or T cell receptor gene, respectively..

Claim 109 is further limiting with the additional limitation that the method of analysis is based on reading of the labeled amplified DNA.

The top of column 2 on page 6512 of Faure et al. teaches RNA extraction and cDNA synthesis (i.e. instant claim 54 and the first part of claim 55).

The section in column 2 of page 6512 of Faure et al., entitled "Determination of the C  $\kappa$ -specific public T cell repertoire with immunoscope," (lines 15-45) describes the remainder of the instant set of claims. Specifically, this passage of Faure et al. recites use of PCR on constant regions of the DNA, use of fluorescent tags to label amplified DNA, run-off reactions, and electrophoresis. Figure 3 of Faure et al. illustrates the results from electropherograms identifying peaks and illustrating their positions and areas.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the T cell repertoire data by use of the smoothing algorithm of data peaks in Sotak et al. wherein the motivation would have been that the algorithms provided on page 786 of Sotak et al. provides means for simplifying spectral data to more conveniently evaluate peak area. There would have been a reasonable expectation of success in combining the study of Faure et al. with the algorithm of Sotak et al. because the peak smoothing algorithms in Sotak et al. are generically applicable to any type of spectral data, including the data regarding T cell repertoires of Faure et al.

### ***Response to Arguments***

Applicant argues that the amendments and cancellation of the rejected claims overcomes the rejection of record. It is noted that the previous rejections have been withdrawn in view of cancellation of previously pending claims. In order to facilitate prosecution, however, arguments regarding Faure et al. are addressed as follows. In

response to the argument that Faure et al. does not teach the instantly recited method, it is noted that the combination of Faure et al. and Sotak et al. does teach all of the claimed limitations, including a peak smoothing algorithm, as set forth above.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

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(November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)).

The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/  
Russell S. Negin, Ph.D.  
2 July 2008

/Marjorie Moran/  
Supervisory Patent Examiner, Art Unit 1631